WNT3A promotes myogenesis of human embryonic stem cells and enhances in vivo engraftment.

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Funding Grants: A Novel Microenvironment-Mediated Functional Skeletal Muscle from Human Embryonic Stem Cells and their In Vivo Engraftment, Technologies to improve in vivo function of transplanted stem cells

Public Summary:
This study describes WNT3A induced myogenic differentiation of human embryonic stem cells. When transplanted in vivo these hESC-derived cells exhibited survival and engraftments. The cells contributed to the regeneration of damaged muscle fibers and the satellite cell compartment

Scientific Abstract:
The ability of human embryonic stem cells (hESCs) to differentiate into skeletal muscle cells is an important criterion in using them as a cell source to ameliorate skeletal muscle impairments. However, differentiation of hESCs into skeletal muscle cells still remains a challenge, often requiring introduction of transgenes. Here, we describe the use of WNT3A protein to promote in vitro myogenic commitment of hESC-derived cells and their subsequent in vivo function. Our findings show that the presence of WNT3A in culture medium significantly promotes myogenic commitment of hESC-derived progenitors expressing a mesodermal marker, platelet-derived growth factor receptor-alpha (PDGFRA), as evident from the expression of myogenic markers, including DES, MYOG, MYH1, and MF20. In vivo transplantation of these committed cells into cardiotoxin-injured skeletal muscles of NOD/SCID mice reveals survival and engraftment of the donor cells. The cells contributed to the regeneration of damaged muscle fibers and the satellite cell compartment. In lieu of the limited cell source for treating skeletal muscle defects, the hESC-derived PDGFRA(+) cells exhibit significant in vitro expansion while maintaining their myogenic potential. The results described in this study provide a proof-of-principle that myogenic progenitor cells with in vivo engraftment potential can be derived from hESCs without genetic manipulation.